

# Morbidity associated with MDMA (ecstasy) abuse: A survey of emergency department admissions

Pinchas Halpern<sup>1</sup>, Jenny Moskovich<sup>2</sup>, Beni Avrahami<sup>3</sup>,  
Yedidia Bentur<sup>4</sup>, Dror Soffer<sup>5</sup>, and Kobi Peleg<sup>2</sup>

## Abstract

**Methods:** We conducted a prospective, representative-sample nationwide study on morbidity related to 3,4, methylenedioxymethamphetamine (MDMA; 'ecstasy') as determined from admissions to 5 geographically representative emergency departments (EDs) and from data from the poison information center (PIC). MDMA-related ED admissions were analyzed over a 7-month period and the records of all PIC calls were reviewed. **Results:** There were 52 (age 15–44 years, 32 males) ecstasy-related ED admissions during the study period. Most (68%) admissions presented to the ED at night, 52% on weekends and 44% consumed the drug at clubs and parties. Forty-six percent of the patients took between 1/2 to 3 tablets and 29 patients (56%) had taken ecstasy before. Twenty-two subjects (42%) reported poly-drug use. Fifteen subjects (29%) required hospitalization, six of them (11%) to the intensive care unit. The most common manifestations were restlessness, agitation, disorientation, shaking, high blood pressure, headache and loss of consciousness. More serious complications were hyperthermia, hyponatremia, rhabdomyolysis, brain edema and coma. **Conclusion:** The image of ecstasy as a safe party drug is spurious. The results of this study confirm that the drug bears real danger of physical harm and of behavioral, psychological and psychiatric disturbances.

## Keywords

ecstasy, emergency admissions, Israel, morbidity, nationwide survey

## Introduction

The use of the illicit drug 3,4, methylenedioxymethamphetamine (MDMA; 'ecstasy') has been constantly increasing. Reports indicate a direct association between physical and mental injury and mortality and complications from taking the drug, especially among young people.<sup>1,2</sup> Users of the drug regard it as harmless, with minimal side effects and not habit-forming,<sup>3</sup> but clinical experience testifies to numerous physical and psychological side effects of its use. The symptomatic characteristics of the drug cause high blood pressure, increased pulse rate and sleep disturbances. Its psychological effects include dulling of the senses, depression, anxiety, anger, aggression and exhaustion. Other possible phenomena are confusion and loss of judgment.<sup>4,5</sup> In the long run, ecstasy users may suffer psychiatric problems such as paranoia and hallucinations for up to 2 years from the time of use.<sup>6</sup> Long-term effects including panic attacks, depression, sleep disorders, suicidal

ideation and psychosis have also been reported.<sup>7,8</sup> Animal experiments have produced varied results. A

<sup>1</sup> Department of Emergency Medicine, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

<sup>2</sup> National Center for Trauma and Emergency Medicine Research, Gertner Institute for Health Policy and Epidemiology, Ramat Gan, Israel

<sup>3</sup> Addictions Authority - Drugs, Alcoholism, Prisoners Rehabilitation, Homeless, Municipality of Tel Aviv-Jaffa, Tel Aviv, Israel

<sup>4</sup> Israel Poison Information Center, Rambam Health Care Campus, the Bruce Rappaport Faculty of Medicine, The Technion, Haifa, Israel

<sup>5</sup> Trauma Unit, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

## Corresponding author:

Pinchas Halpern, Department of Emergency Medicine, Tel Aviv Sourasky Medical Center, 6 Weitzman Street, Tel Aviv 64239, Israel

E-mail: dr\_halperin@tasmc.health.gov.il

recent analysis of rat studies concluded that ecstasy is capable of causing neurotoxicity at relatively high doses (e.g. >25 mg/kg, compared to usual human consumption doses of 1–2 mg/kg/dose), with injury both to 5, hydroxytryptamine (5-HT) neurons and to non 5-HT neurons as well as induce persistent increases in anxiety-like behaviors in rats without measurable 5-HT deficits, which suggests that even moderate doses may pose risks.<sup>9</sup> Since the end of the 1980s, numerous ecstasy-related deaths have been reported in the medical literature, mostly due to hyperthermia, typically accompanied by disseminated intravascular coagulation (DIC), extreme dehydration and liver or renal failure.<sup>10–12</sup> Death can also occur as a result of hyponatremia due to a syndrome of inappropriate antidiuretic hormone (SIADH) and excessive water intake.<sup>13</sup> What is most alarming is that drugs such as these have reached, what some consider, epidemic proportion.<sup>14</sup> At the same time, there are those who feel ecstasy is not harmful, especially when used in a controlled manner for therapeutic purposes. Thus, a prospective Dutch study<sup>15</sup> compared 25 subjects before and after a mean of two ecstasy pills to 24 ecstasy-naïve subjects and found no difference in cognitive function with functional magnetic resonance imaging (fMRI). The same lead author, however, found that heavy ecstasy use (mean 322 pills lifetime) was associated with various memory performance impairments on fMRI.<sup>16</sup>

The first known use of ecstasy in Israel was in 1988, and the drug was outlawed in 1991. About 30,807 tablets were confiscated by the authorities in 1978, 150,000 in 1998, 464,651 in 1999 and 260,000 tablets between January and November in 2000.<sup>17</sup> The latest (2001) survey of the Israel Anti-Drug Authority showed that 2.7% of Israeli teenage students (i.e. 7th to 12th graders) reported using ecstasy in the past year compared to 2.6% in 1995, while among adults, aged 18–40 years, the reported rate was 1.3% in 2001 compared to 0.9% in 1995.<sup>18</sup>

Both in Israel and world-wide, no firm data exist on ecstasy-associated morbidity. Such information is essential for the agencies responsible for dealing with the growing phenomenon in order to develop educational, preventative and therapeutic programs. In an effort to provide these guidelines and with the cooperation of a representative sample of general hospitals throughout the country and the national Israel Poison Information Center (IPIC), we were able to design an investigation based on a number of selected parameters that could reflect the extent of significant morbidity throughout an entire country. The cohort of this

prospective study consists of ecstasy users whose reaction to the drug was severe enough to motivate their arrival to hospital ED.

## Methods

Prospective data were collected from emergency departments (EDs) in five Israeli medical centers that are geographically distributed throughout the county: the Sourasky Medical Center in Tel Aviv and the Sapir Medical Center in Kfar Saba (central); Soroka Medical Center in Beersheva, Barzilai Medical Center in Ashkelon and Yoseftal Hospital in Eilat (southern). In addition, reports were received from the IPIC, which also includes all cases from Rambam Hospital (north) and Bikur Holim (Jerusalem). The study was approved by the Institutional Review Board of the Tel Aviv Medical Center. Data collection took place during the 7-month period between August 2002 and February 2003.

Patients were identified as having an ecstasy-associated complaint by the medical staff of the ED. A physician or nurse was assigned to be a research coordinator for each participating department. A sample of the data forms had been displayed on bulletin boards, and the coordinator met with emergency staff members in order to reinforce the knowledge of the signs and symptoms and typical circumstances of suspected ecstasy use, to report suspected users of ecstasy and record the physical or psychological side effects that appeared to have been directly associated with use of the drug. A national research coordinator (PH) was also appointed for ongoing contact with the hospital coordinators.

The expectation was that the primary challenge would be in identifying which among the arrivals to the ED were ecstasy users. The national coordinator was responsible for gathering the required data according to the study design, following-up on the data collection process and obtaining the full cooperation of all the relevant staff members in the participating hospitals.

Morbidity was identified according to the subject self-report and in most of the cases also to the finding of MDMA in urine (SureStep; Applied Biotech, San Diego, California, USA). This type of kit can give a specific indication for ecstasy. Concomitant alcohol or other drug use was identified through blood tests.

## Data collection

Patients were identified either by self-reporting ecstasy use or by the patient's response to specific

questions asked by the medical staff. Of the 52 patients who reported ecstasy use, 29 (56%) underwent a urine test for ecstasy. No drug blood tests were performed. Information was gathered from medical records and through interviews with patients as to the circumstances related to their taking ecstasy. The details recorded in the patients' medical records were retrieved from the system by the local ED study coordinator. They were entered on a specifically designed form that was completed in real time by the doctor or nurse and faxed within 24 hours by the local ED study coordinator to the national research coordinator who entered them into a computerized system which produced statistical results through the use of the SAS statistical package (SAS Institute Inc. Cary, North Carolina, USA).

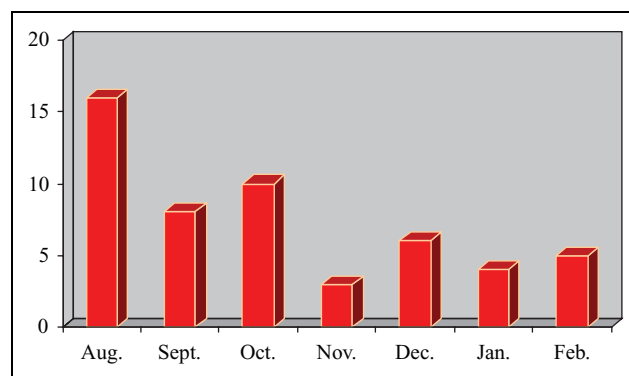
The information on the form included age, gender, city/town of residence, citizenship status, date and hour of arrival at the ED, means of transportation to the ED, ED disposition, length of stay in hospital, injury type, patient disposition, circumstances surrounding the use of ecstasy (date, day of the week, hour, quantity, past use, location and nature of the event) and concomitant drug or alcohol use. Documentation of referrals to the IPIC due to poisoning from ecstasy use was provided on the Institute's standard structured toxicological forms. This documentation also included a follow-up of each patient until discharge from the hospital. IPIC patients were identified by their name and ID numbers in order to avoid duplicate recording of patients reported by both the IPIC and the EDs of the participating hospitals.

## Results

During the 7-month study period, a total of 52 ED patients were identified as suffering from ecstasy-related morbidity by the ED staff of five general hospitals ( $n = 34$ ) and through the IPIC database ( $n = 18$ ). The breakdown of these numbers by hospital were Rambam – 12, Soroka – 11, Yoseftal – 10, Tel Aviv Sourasky – 6, Barzilai – 5, Sapir – 2, Beilinson – 2, Naharyia – 1, Bikur Holim – 1, Ha Emek – 1 and Hillel Yaffe – 1.

The rate of ecstasy-related ED visits, from the total number of ED visits during the study period, was 0.012 (a total of 440,444 ED visits).<sup>19</sup>

The distribution of cases during the 7-month study period was not uniform, with significantly higher numbers being recorded in August than during the other months (Figure 1). The gender breakdown of the



**Figure 1.** Number of ecstasy cases per month.

subjects was 33 (63%) males and 19 (37%) females whose ages ranged from 15 to 44 years (mean = 24.2 years, SD = 6.3). Almost one-third ( $n = 16$ , 31%) were younger than 20 years, one-half ( $n = 26$ ) were 20–30 years old, 15% ( $n = 8$ ) were older than 30 years and the age of two subjects was unknown. Seven (13%) subjects were university students and seven were public school pupils. Of the 32 subjects older than 21 years of age, 15 (47%) reported being employed. Twenty-three (52%) came from large cities, 15 (29%) from medium- and small-sized communities and seven (13%) from Eilat, a seaside resort city in the southernmost tip of Israel. The residence of seven subjects was not known.

More than one-half ( $n = 27$ , 52%) (no data were available for five subjects) of all episodes occurred during the weekend (Friday and Saturday in Israel). Information on the time of use was obtained for 37 cases – 25 (68%) subjects took the drug between 23:00 and 03:00.

The amount of ecstasy tablets reportedly consumed ranged from one-half tablet to 15 tablets. No analysis of drug used was available. Twenty-four patients (46%) consumed 0.5 tablets, 10 patients (19%) took 4–8 tablets, three (6%) took 14–15 tablets, four (8%) reported taking 'many' tablets and 11 (21%) did not know how many tablets they had taken. Twenty-two subjects (42%) concomitantly used other substances, alcohol ( $n = 11$ ) and other illicit drugs ( $n = 11$ : opiates – 3, cocaine – 2, cannabis – 3, benzodiazepines – 2, LSD – 1). Only in 12 cases (23%), ecstasy was the only substance reported used and 18 did not report on this issue.

Nine (17%) patients claimed that this was their first use of ecstasy, while 23 (44%) reported having used ecstasy in the past. This information was not available for the other 20 patients. There was no correlation

**Table 1.** Circumstances of use of Ecstasy (*N* = 52)

Day of week	<i>N</i> (%)
Sunday	4 (8)
Monday	3 (6)
Tuesday	3 (6)
Wednesday	6 (11)
Thursday	4 (8)
Friday	14 (27)
Saturday	13 (25)
Unknown	5 (9)
Time of day of usage	
Night	25 (68)
Day	12 (23)
Unknown	15 (29)
Venue	
Club	15 (29)
Private party	8 (15)
Outdoor party	6 (12)
Home alone	10 (19)
Suicide attempt	2 (4)
Other	3 (6)
Unknown	8 (15)
Location	
Urban	42 (81)
Rural	5 (9.5)
Unknown	5 (9.5)
Number of tablets, <i>n</i>	
0.5-1	11 (21)
1.5-3	13 (25)
4-6	7 (13)
7-8	3 (6)
14-15	3 (6)
Unknown	15 (29)
Previous use	
Yes	23 (44)
No	9 (17)
Unknown	20 (38)
Other substance use	
Ecstasy only	12 (23)
Additional drugs	11 (21)
Alcohol	11 (21)
Unknown	18 (35)

**Table 2.** Mode and time of arrival (*N* = 52)

Time of arrival	<i>N</i> (%)
Night shift (2300-0700)	22 (42)
Day shift (0700-0300)	18 (35)
Evening shift (1500-2300)	10 (19)
Unknown	2 (4)
Transportation	
Private car	24 (46)
Regular ambulance	14 (27)
Intensive care ambulance	10 (19)
Other	3 (6)
Unknown	1 (2)

**Table 3.** Emergency department disposition (*N* = 52)

Disposition	<i>N</i> (%)
Discharge	27 (52)
Hospitalization	15 (29)
Self discharge	7 (13)
Unknown	3 (6)
Hospitalization	
Intensive care unit	6 (11.5)
Internal medicine ward	5 (10)
Pediatrics	2 (4)
Psychiatry	1 (2)
Unknown	1 (2)

(13%) patients discharged themselves against medical advice (Table 3). Fifteen (29%) patients required hospitalization, of whom six were sent to the ICU. No information on disposition was available for three patients.

### Clinical features

There was a wide range of physical, physiological and psychiatric effects of the use of ecstasy among the 52 study patients (Table 4). The most common manifestations were restlessness, agitation, disorientation, shaking, high blood pressure, headache and loss of consciousness. The more serious complications were hyperthermia (rectal temperature greater than 39°C), hyponatremia (serum sodium less than 130 mmol/L), rhabdomyolysis (serum Creatine Kinase greater than 1500 units), brain edema (on CT scan) and coma. All patients with rhabdomyolysis, hyperthermia or coma (or any combination thereof) were admitted to the ICU. About 85% of the subjects suffered some physical manifestations, of which 69% had more than one physical symptom or sign. A total of 73% of the subjects

between the number of tablets taken at the index event and previous use of ecstasy.

The settings in which the drug was used are listed in Table 1. The most common time of presentation to an ED was between 23:00 and 07:00 (Table 2). The mode of transportation to an ED is listed in Table 2; more (38%) of the patients who arrived by ambulance were hospitalized and/or admitted to an intensive care unit (ICU) than those who arrived in private cars (17%).

Twenty-seven patients (52%) were discharged home after initial clinical assessment and seven

**Table 4.** Physical and neuropsychiatric manifestations (*n* = 52)

Physical manifestations	N (%)
Shaking	12 (23)
High blood pressure	11 (21)
Headache	10 (19)
Loss of consciousness	7 (13)
Dehydration	6 (12)
Faintness	6 (12)
Stroke	5 (10)
Tachycardia	5 (10)
Dilated pupils	5 (10)
Nausea	4 (8)
Coma	4 (8)
Sweating	3 (6)
Rhabdomyolysis	3 (6)
Hyperthermia	3 (6)
Hyponatremia	3 (6)
Blurred vision	3 (6)
Epileptic seizure	2 (4)
Dizziness	2 (4)
Abdominal pain	2 (4)
Pneumonia	2 (4)
Coagulopathy	1 (2)
Brain edema	1 (2)
Respiratory arrest	1 (2)
Paresthesiae	1 (2)
Muscle cramps	1 (2)
Cyanosis	1 (2)
Neuropsychiatric effects	
Psychomotor agitation	20 (38)
Anxiety	15 (29)
Disorientation, cognitive disturbances	13 (25)
Mood changes	10 (19)
Psychotic disturbances	9 (17)
Suicidal ideations	7 (13)
Panic attacks	5 (10)
Logorrhea	5 (10)
Verbal expression of psychological distress	5 (10)
Inappropriate facial expressions	4 (8)
Depression	4 (8)
Incoherent speech	4 (8)
Illusions	3 (6)
Excessive empathy	4 (8)
Paranoia	2 (4)
Associative speech	2 (4)
Memory disturbances	1 (2)
Violence	1 (2)

experienced some behavioral or psychiatric disturbances and 52% of them had more than one such disturbance.

## Discussion

According to the Israel Anti-Drug Abuse Foundation, 22,700 persons (aged 12–40) used ecstasy during ‘the previous month’ in 2001 in Israel.<sup>18</sup> Thus, the rate of ecstasy-related morbidity is, at least, 0.23, since not all hospitals in Israel were included in the study.

The results of this nationwide study illustrate the severe morbidity associated with the use of ecstasy and serve to shatter the myth that there is little or no risk in using it. Ecstasy is known as a ‘club drug’ and its use is usually associated with recreational settings, parties, raves and clubs for relatively young people.<sup>20</sup> In Australia, 76% of rave participants were found to have tried ecstasy,<sup>21</sup> and Schifano et al. recently reported from the UK that they identified 605 ecstasy-related deaths over a 10-year period (1997–2007), typically in young, healthy persons, mostly not known drug users.<sup>22</sup> Degenhardt et al.<sup>23</sup> reported from Australia, using multiple sources, that ecstasy use had increased in adults, poly-drug use and prolonged use were more common, but the percentage of ecstasy users seeking medical help was low and usually consisted of subjects seeing their general practitioner for support or treatment of drug-related problems. Sixty-five percent of rave-goers in Canada reportedly tried it,<sup>24</sup> and about 60% of club-goers in Italy reported using it.<sup>25</sup> There are no data on ecstasy use by party-goers in Israel, but the 2001 survey of the Israeli Anti-Drug Authority shows that about 25% of teenage students attend parties.<sup>18</sup>

The Drug Abuse Warning Network,<sup>26</sup> operating in the US since the 1970s, is a system that monitors and provides essential information on morbidity and mortality related to the use of drugs throughout the US. Data on patients who arrived for treatment as a result of the use of illegal drugs or the non-medical use of legal drugs are collected from emergency medicine departments. In 2002, 670,307 people arrived at EDs as a result of drug use (about 1% of all ED visits), of which 8127 (1.2%) were due to ‘club drugs’ use. Ecstasy, the most common ‘club drug’ in 2002, was related to 4026 of these ED visits. Of these patients, 72% used multiple drugs concomitantly. DAWN showed an increase of 856% in ED visits due to ecstasy use between 1995 and 2002 (from 421 to 4026 annually). The peak number of ED visits was 5542 in 2001.

In their report on ecstasy use in Australia, Topp et al. found that the physical and psychological damage to poly-drug users, including interpersonal and



employment problems, is higher than for ecstasy-only users.<sup>27</sup> Williams et al. retrospectively reviewed computerized reports of 48 patients at the ED of the Saint Thomas Hospital in London.<sup>28</sup> All were in the 15–30 years age group, having consumed the drug at the night club. Poly-drug use was common. A wide range of adverse clinical features was found. Richards et al. conducted a 6-month retrospective study in a large municipal hospital in California and emphasized the connection between ecstasy use and trauma injuries.<sup>29</sup> A retrospective study by Sanjurjo et al. in a Barcelona, Spain, reported on 230 ecstasy users who were admitted to the ED for anxiety, uneasiness, cognitive disturbances, motor disturbances and unconsciousness between 2000 and 2002.<sup>30</sup> Two major studies have made methodical and comprehensive efforts to estimate the number of ecstasy-related deaths. The first, in England and Wales, used the database of the National Program on Substance Abuse Deaths (NPSAD). NPSAD maintains a database, which is continually updated with information from coroners' reports on drug-related deaths. Between August 1996 and April 2002, there were 202 cases of ecstasy-related deaths (an average of 3.4 events per month), with a significant increase in incidence over the years.<sup>31</sup> The second study, conducted in New York City between 1997 and 2000, was based on post-mortem data: it reported that MDMA was found in 22 bodies.<sup>32</sup>

Most published studies on ecstasy use concentrate on its epidemiology and on specific morbidity. Few studies have looked nationally at the burden of acute disease caused by ecstasy. Previous evaluations of the extent of morbidity from substance abuse (alcohol and drugs) documented in ED records in Israel had been confined to one or two local hospitals, with no particular attention paid to ecstasy. In 1999–2000, Neumark et al.<sup>33</sup> performed the first prospective survey of admissions to the ED for alcohol and drug use at two hospitals.<sup>28</sup> A study conducted at one hospital focused on the clinical and demographic characteristics of children and youth, aged 12–18 years, admitted to the ED due to the use of alcohol and drugs.<sup>34</sup> Ben-Abraham et al. reported three patients who were hospitalized in the ICU after having taking 1–3 150 mg ecstasy pills and subsequently presenting signs of hyponatremia, high fever, dehydration, rhabdomyolysis and metabolic acidosis accompanied by impaired liver and renal function.<sup>35</sup>

In the present study, we sought to determine the rate of morbidity associated with the use of ecstasy on a national level. Interestingly, our results showed a

relatively high rate of ecstasy-related morbidity in Eilat, a small city of 45,000 residents, with the smallest hospital among those that participated. We suspect that this finding may be related to the fact that Eilat is a resort city whose reputation as an intense 'party city' and its proximity to the Egyptian border make illicit drugs, such as ecstasy, relatively easily accessible. The finding that 16 (31%) of all the incidents occurred in August, as opposed to 3–10 in each of the other study months, is probably due to a larger use of ecstasy during the summer months when school is out and parties are frequent. A more extensive use can reasonably be expected to result in more frequent adverse reactions, in line with the findings of Neumark et al. who showed that more patients came to Israeli hospitals due to alcohol or drug use in August than in any other month.<sup>28</sup> Further support comes from the study of Schifano et al., which reported that a large portion of ecstasy-related deaths occurred in the summer months.<sup>31</sup>

As was found in two other reports based on information from EDs,<sup>23,24</sup> our study reveals that more subjects (63%) were male, unlike the DAWN studies that showed an equal percentage of men and women visiting an ED due to ecstasy poisoning.<sup>21</sup> It is impossible from our data to ascertain whether this gender disparity is due to greater use, use of larger doses or perhaps greater susceptibility of males compared to females. Much larger studies may be needed to answer this question. The patients were 15–44 years old, with an average age of 24 years. About 65% of those harmed by ecstasy were under the age of 26 years, similar to the 75% rate in the US<sup>26</sup>). Despite the general belief that ecstasy users are only young people under 30 years of age, 15% of the subjects in the current study were older than 30 years, raising the suspicion that the use of the drug by older individuals has increased over the past few years. This assumption is supported by an Australian study which showed that ecstasy users ranged in age from 15 to 46 years.<sup>27</sup>

Despite the popular image of ecstasy as a safe party drug, the present study documents that the use of ecstasy carries with it the danger of physical harm and occurrence of behavioral, psychological and psychiatric disturbances. Given that not all Israeli hospitals participated in this study, it is reasonable to assume that the extent of morbidity from use of ecstasy is even higher than reported. The difficulty in attributing ecstasy as the direct cause of the side effects stems from the common concomitant use of other drugs, although the typical symptoms of ecstasy make its clinical diagnosis fairly easy.

Notably, injury may occur with the use of one or two tablets, even with the first one ever ingested. The physical and behavioral-psychiatric symptoms documented in this study are similar to those found by Williams et al.<sup>28</sup> in their study of 48 patients in a London Hospital. All the subjects, with the exception of one fatality, were released after treatment in the ED or after a relatively short hospitalization. Nevertheless, the authors support the position that ecstasy use can have in serious and even life-threatening sequelae. ED personnel must be alert to the fact that when young people arrive in the late hours on a weekend with symptoms that include anxiety, restlessness, confusion, panic, shaking, headache, weakness, dizziness, hypertension, tachycardia etc., the possibility of ecstasy use must be considered in the clinical diagnosis, laboratory assessment ordered and treatment. It is worth stressing once more that the clinical picture is likely to be complicated by multiple-drug ingestion, thus posing greater diagnostic, toxicological analysis and management challenges for the ED staff that typically represent the front-line response for ecstasy and other 'club drugs'-related problems. Although it is difficult to isolate ecstasy as the cause of injury, it is likely, as suggested by Schifano et al., that when taken with other drugs, ecstasy has a 'facilitating role' in causing damage and even death.<sup>31</sup> In the majority of our cases in which the data about previous use of ecstasy was known, the drug-related injury occurred at the time of repeated use. This was also demonstrated in the study by Williams et al.<sup>28</sup> This suggests that prior uneventful use of ecstasy does not guarantee future problem-free use. This point is critical in regard to educational and consciousness-raising planning and needs to be reinforced in health promotion and drug awareness/educational material.

## Study limitations

Although this study may not represent the full extent of ecstasy morbidity in the country, the sample can be considered representative due to the broad base of participating hospitals together with the inclusion of reports by the IPIC. Particularly challenging is the identification of patients who arrive at the ED due to ecstasy use, but who do not volunteer information about their ecstasy consumption, they may have slipped through the net. The study period was long enough for it to be representative, yet did not reach the usual 12-month duration because of budget constraints.

In conclusion, Israel is a characteristic western country and we believe that our current findings on morbidity associated with the use of ecstasy can be extrapolated to reflect the situation of most other western nations. We found significant morbidity associated with the use of ecstasy. Current Israeli law does not require that medical staff report treating patients for ecstasy abuse, though it is considered a class-one controlled substance.

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